

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
7 November 2002 (07.11.2002)

PCT

(10) International Publication Number  
**WO 02/087423 A3**

(51) International Patent Classification<sup>7</sup>: **A61K 31/417**,  
31/4172, 31/198

(21) International Application Number: PCT/US02/13784

(22) International Filing Date: 2 May 2002 (02.05.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
60/287,721 2 May 2001 (02.05.2001) US

(71) Applicant (for all designated States except US):  
**BLANCHETTE ROCKEFELLER NEURO-  
SCIENCES INSTITUTE** [US/US]; 9601 Medical  
Center Drive, Rockville, MD 20850 (US).

(71) Applicants and

(72) Inventors: **ALKON**, Daniel [US/US]; 6701 Bonaventure  
Court, Bethesda, MD 20817 (US). **SUN**, Miao-Kun  
[US/US]; 16012 Howard Landing Drive, Bethesda, MD  
20878 (US).

(74) Agent: **GOLLIN**, Michael, A.; **VENABLE**, BAETJER,  
HOWARD & CIVILETTI, LLP, 1201 New York Avenue,  
NW, Suite 1000, P.O. Box 34385, Washington, DC 20043-  
9998 (US).

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,  
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,  
CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,  
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,  
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,  
MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG,  
SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ,  
VN, YU, ZA, ZM, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM,  
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),  
Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),  
European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR,  
GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent  
(BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,  
NE, SN, TD, TG).

**Published:**

- with international search report
- before the expiration of the time limit for amending the  
claims and to be republished in the event of receipt of  
amendments

(88) Date of publication of the international search report:  
27 February 2003

For two-letter codes and other abbreviations, refer to the "Guid-  
ance Notes on Codes and Abbreviations" appearing at the begin-  
ning of each regular issue of the PCT Gazette.



**WO 02/087423 A3**

(54) Title: CARBONIC ANHYDRASE ACTIVATORS FOR ENHANCING LEARNING AND MEMORY

(57) Abstract: The invention provides a method for improving attentive cognition comprising administering a compound that po-  
tentiated intraneuronal carbonic anhydrase activity thereby improving establishment of a theta rhythm.

INTERNATIONAL SEARCH REPORT

PCT/US02/13784

**Continuation of B. FIELDS SEARCHED Item 3:**

Databases Searched: EAST, CAPLUS, MEDLINE

Search Terms: carbonic anhydrase, imidazole, alanine, phenylalanine, phenethylamine, histamine, histidine, triazole, cognition, cognitive, learn, learning, learned, Alzheimer, stroke, hypoxia, ischemia, and brain.

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US02/13784

## CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 31/417, 31/4172, 31/198

US CL : 435/325, 183, 424/78.15, 514/2, 176, 359, 396, 631, 638, 235.8

According to International Patent Classification (IPC) or to both national classification and IPC

## FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/325, 183, 424/78.15, 514/2, 176, 359, 396, 631, 638, 235.8

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
Base See Continuation Sheet

## DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X, P	SUN et al. Pharmacological Enhancement of Synaptic Efficacy, Spacial Learning, and Memory through Carbonic Anhydrase Activation in Rats. Pharmacology And Experimental Therapeutics. June 2001, Vol. 297, Issue 3, pages 961-967, see entire document.	1-19
Y, P	WO 01/93744 A2 (THE GOVERNMENT OF THE UNITED STATES OF AMERICA, as represented by THE SECRETARY OF HEALTH AND HUMAN SERVICES) 13 December 2001 (13.12.2001), see entire reference.	1-19
Y	SUN et al. Theta Rythum of Hippocampal CA1 Neuron Activity: Gating by GABAergic Synaptic Depolarization. The Journal of Neurophysiology. January 2001, Vol. 85, No.1, pages 269-279, see entire document.	1-18
Y	SUPURAN et al. Carbonic Anhydrase Activators: Synthesis of High Affinity Isozymes I, II, and IV Activators, Derivatives of 4-(arylsulfonylureido-amino acyl)ethyl-1H-imidazole. Enzyme Inhibition. 2000, Vol. 15, No.5, pages 471-86, see abstract.	1-19

☒ Further documents are listed in the continuation of Box C.

See patent family annex.

## Special categories of cited documents:

- document defining the general state of the art which is not considered to be of particular relevance
- earlier application or patent published on or after the international filing date
- document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- document referring to an oral disclosure, use, exhibition or other means
- document published prior to the international filing date but later than the priority date claimed

"T"

later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X"

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y"

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&amp;"

document member of the same patent family

Date of the actual completion of the international search

October 2002 (01.10.2002)

Date of mailing of the international search report

18 DEC 2002

Name and mailing address of the ISA/US

Commissioner of Patents and Trademarks  
Box PCT  
Washington, D.C. 20231

Authorized officer

Clinton Ostrup

Facsimile No. (703)305-3230

Telephone No. (703) 308-1235

in PCT/ISA/210 (second sheet) (July 1998)

## INTERNATIONAL SEARCH REPORT

## (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	BRIGANTI et al. Carbónic Anhydrase Activators: X-ray Crystallographic and Spectroscopic Investigations for the Interaction of Isozymes I and II with Histamine. Biochemistry. 1997, Vol. 36, pages 10384-10392, see entire document.	1-18
Y	WO 85/03869 A1 (ERK, VERNON) 12 September 1985 (12.09.1985), See entire reference.	1-19
Y	EP 0 387 867 A1 (G.D. SEARLE & CO.) 19 September 1990 (19.09.1990), see entire reference.	1-19
Y	US 5,972,684 A (BANDMAN et al) 26 October 1999 (26.10.1999), see, col. 2, lines 11-68, col. 3 lines 1-37, col. 20, lines 51-62, col. 21, lines 17-29.	1-19